Remarks

Applicant requests reconsideration on the merits of the above-referenced patent application.

I. Claim Amendments

Claim 20 is pending. This amendment amends claim 20. Applicant submits that this amendment does not introduce any new matter. Specifically:

In accordance with the Examiner's suggestion, "*A. pleuropneumoniae* RTX-" has been replaced with "*Actinobacillus pleuropneumoniae* repeat in toxin". This amendment is supported by Applicant's specification at, for example, lines 9-10 on page 1, and lines 25-26 on page 15.

Claim 20 also has been amended to expressly recite the presence of a heterologous gene that is functionally linked to the promoter region. This is supported by Applicant's specification at, for example, page 9, lines 16-25.

Other amendments rephrase claim 20. Applicant submits that such amendments are permissible under MPEP §2163.07.

Applicant requests that all the claim amendments be entered because they only require cursory review by the Examiner and place the claims in better condition for allowance or will reduce the issues on appeal. See MPEP §§714.12 & 714.13. In addition, Applicant notes that the amendment spelling out the full name of "*A. pleuropneumoniae* RTX" should be added as a matter of right, given that it complies with the suggested language in Paragraph 4 of the August 24, 2005 Office action. See MPEP §714.12.

Applicant reserves the right to pursue any canceled subject matter and/or any other subject matter disclosed in this application in one or more divisional and/or continuation applications.

II. Acknowledgment of withdrawal of rejections as to claims 7-9

The March 29, 2005 Office action rejected claims 7-9 under 35 U.S.C. §112 (first and second paragraphs), 35 U.S.C. §101, and 35 U.S.C. §102(b). Applicant acknowledges that these rejections have been withdrawn in view of the claim cancellations.

III. Response to 35 U.S.C. §112 (first paragraph) rejection in Paragraph 3 of Office action

Claim 20 has been rejected under 35 U.S.C. §112 (first paragraph) as lacking written description. Applicant respectfully requests withdrawal of this rejection.

Claim 20 stems from Applicant's discovery that the ApxIV promoter is a switchable promoter that switches off *in vitro* and switches on *in vivo*. See Applicant's specification, page 9, lines 31-32. This feature makes the promoter a versatile expression tool both in its natural host and other bacteria. See Applicant's specification, page 9, line 32 to page 10, line 1. For example, several proteins are toxic if they are expressed in bacteria to which they are foreign. Consequently, a heterologous gene encoding such a protein generally cannot be introduced into foreign carrier bacteria because successful recombinants ultimately die as a result of the expression of the gene. See Applicant's specification, page 8, lines 29-33. Applicant's promoter provides a mechanism for addressing this problem. Specifically, the promoter can be used to govern the expression of a heterologous gene encoding a protein that is toxic to its desired bacteria carrier. Because the promoter is turned off while the carrier is *in vitro*, it can be used to suppress expression of the gene so that the carrier can be grown to high densities *in vitro* without producing the protein. Once the desired amount of carrier is produced, the carrier can be administered to the host. At that point, the carrier will begin expressing the gene, and, at some point during replication or after death of the carrier, the protein will become available to the immune system of the host. See Applicant's specification, page 9, lines 8-15. Thus, the promoter suppresses production of the toxic protein during the growth of the carrier so that the carrier can populate, and then initiates production of the protein once the carrier is administered to the host.

Applicant submits that claim 20 is supported by the written description. Claim 20, after all, recites the sequence believed to comprise the ApxIV promoter (*i.e.*, from position 594 to 641 of SEQ ID NO: 5). Applicant submits that this complies with the Federal Circuit's recent decision, Capon v. Eshhar, 76 USPQ2d 1078 (Fed. Cir. 2005). In that case, the Court held that 35 U.S.C. §112 (first paragraph) does not *per se* prohibit open claiming of nucleotide sequence to the extent the invention relates to a novel combination of DNA segments to achieve a novel result rather than to the DNA sequences themselves. See Capon, pages 1084-85. Other legal precedent also supports Applicant's position. For example:

- In Ex Parte Fisher, 72 USPQ2d 1020, 1030 (Bd.Pat.App. & Int. 2004) (unpublished), the Board held that the written description requirement was satisfied even though the claim-at-issue included the term "comprising", which allowed for the addition of nucleotides or other molecules at either end of the recited nucleotide sequences.
- In Example 8 on page 26 of the Revised Interim Written Description Guidelines Training Materials (http://www.uspto.gov/web/patents/guides.htm), the written description requirement was found to be satisfied where, *inter alia*, "any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution".
- In Enzo Biochem Inc. v. Gen-Probe Inc., 63 USPQ2d 1609 (Fed. Cir. 2002), the Court adopted the Patent Office's interpretation that the written description requirement is satisfied as long as the "relevant identifying characteristics . . . *i.e.*, complete or partial structure" are provided. *Id.* at 1613 (emphasis added).
- In Singh v. Brake, 65 USPQ2d 1641, 1642 & 1647-50 (Fed. Cir. 2003), the Court affirmed the Board's finding of sufficient written description in the senior party's specification for a count directed to a DNA construct comprising the sequence 5'-L-S-Gene*-3', wherein "L" was characterized generally as encoding a Saccharomyces α-factor leader sequence recognized by a yeast host for secretion; "S" was characterized generally, subject to a proviso, as encoding a spacer sequence providing processing signals resulting in the enzymatic processing by the yeast host of a precursor polypeptide encoded by

> L-S-Gene* into the polypeptide encoded by Gene*, and containing the sequence 5'-R_1-R_2-3' immediately adjacent to the sequence Gene* (R_1 being a codon for lysine or arginine, and R_2 being codon for arginine); and "Gene*" was characterized generally as encoding a polypeptide foreign to Saccharomyces.

Consistent with the above precedent, claim 20 specifically focuses on describing Applicant's contributions. In this instance, Applicant's contributions are the discovery of the switchable promoter, and the novel combination of the promoter with a heterologous gene, which achieves the novel result of suppressing the gene *in vitro* and promoting the gene *in vivo*. Applicant's claim 20 recites the portion of the sequence that Applicant believes to be novel and essential. Specifically, claim 20 recites a well-defined piece of DNA in which the promoter elements and the universal ATG start codon are located. The nucleotides outside the recited sequence will obviously vary, depending on, for example, the protein to be expressed and the presence of non-essential promoter elements that influence promoter efficiency. Applicant's specification provides ample instruction for one skilled in the art to apply the invention within these variations. Applicant has, for example, provided an example sequence (*i.e.*, SEQ ID NO: 5) that illustrates a broader sequence comprising the recited sequence. Applicant has explained the significance of the flanking sequence of the promoter's consensus regions as possibly influencing the efficiency of the promoter. See page 10, lines 15-27. Applicant also has provided instruction for functionally linking the promoter region to a heterologous gene, and using such a moiety. See, e.g., page 8, line 28 to page 10, line 13. And, Applicant has demonstrated the promoter's suppression *in vitro* and promotion *in vivo*. See Examples 4 and 5 on pages 19-20.

Simply put, claim 20 recites Applicant's contributions, *i.e.*, the switchable promoter, and its functional linking to a heterologous gene. The variability within the genus arises from aspects that are not part of Applicant's particular contribution. Moreover, Applicant's specification provides instruction as to these variations, including SEQ ID NO. 5, which illustrates a variation that may exist in the sequence that flanks the consensus regions. Thus, requiring Applicant to further narrow claim 20 would unnecessarily and arbitrarily limit claim

20 to less than Applicant's complete invention. Applicant submits that this rejection should be withdrawn.

IV. Response to 35 U.S.C. §112 (second paragraph) rejection in Paragraph 4 of Office action

Claim 20 has been rejected under 35 U.S.C. §112 (second paragraph) as being indefinite. Applicant respectfully requests withdrawal of this rejection. Per the Examiner's suggestion, Applicant has replaced "*A. pleuropneumoniae* RTX-" with "*Actinobacillus pleuropneumoniae* repeat in toxin". Applicant submits that this amendment moots the rejection.

V. Response to 35 U.S.C. §101 rejection in Paragraph 5 of Office action

Claim 20 has been rejected under 35 U.S.C. §101 as lacking utility. Applicant respectfully requests withdrawal of this rejection. This rejection is based on the concern that claim 20 reads on a naturally occurring sequence. Without making any representation as to merit of this concern, Applicant has amended claim 20 to further define the sequence as including a heterologous gene functionally linked to the promoter region. Applicant believes this amendment moots the Examiner's concern.

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Applicant does not believe that any fee is due in connection with this filing. If, however, Applicant does owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **02-2334**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **02-2334**.

Applicant submits that the pending claim is in condition for allowance, and requests that this application be allowed. The Examiner is requested to call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE

I certify that this correspondence is being sent via facsimile on **November 22, 2005** to facsimile no. **(571) 273-8300** to the attention of **Examiner Jana A. Hines, Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.**

DMG/DAP